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Nosocomial Postsurgical Meningitis in Children: A 12-Year Survey Comparing Data From 1993-1998 With Data From 1999-2004

TO THE EDITOR—The incidence of nosocomial meningitis after neurosurgery is increasing.[1-2] In a previous study, a survey of all 8 pediatric and neonatal neurosurgery departments in Slovakia revealed that 101 cases of pediatric bacterial meningitis were recorded during 1993-1998, with an attributable mortality of 15% and sequelae detected in 18% of cases.[1] We conducted a similar survey during 1999-2004, which revealed an additional 57 cases of disease. Here, cases of pediatric nosocomial meningitis during 1999-2004 are compared with those during 1993-1998 with respect to etiology, risk factors, and outcome.

A prospective protocol was used to assess each case of meningitis that occurred during hospitalization in persons aged 18 years or less at any of the 8 pediatric and neonatal neurosurgery departments in Slovakia; the number of such departments has not changed during the past 10 years. Nosocomial meningitis was clinically defined as onset of meningitis after neurosurgery in patients with a positive result of a cerobrospinal fluid culture. Risk factors were assessed, including the etiology of meningitis, the type of neurosurgery, and the presence of underlying disease(s), trauma, abnormal central nervous system findings, central nervous system disease, positive results of blood cultures, malignancy, and hemorrhage. Mortality rates associated with infection and/or to central nervous system sequelae and treatment (ie, surgery and antibiotics therapy) were assessed, and antimicrobial resistance was measured for the pathogens most commonly isolated from the cerebrospinal fluid of study subjects (coagulase-negative staphylococci [CoNS], *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*). No major changes in surgical techniques (including shunt insertion and prosthe-

TABLE 1. Comparison of the Etiology of Nosocomial Meningitis During the 2 Study Periods

Pathogen	No. (%) of isolates, by period		
	1993-1998 (n = 115)	1999-2005 (n = 75)	P
Gram-positive organisms			
Staphylococcus aureus	10 (8.7)	2 (2.6)	NS
Coagulase-negative staphylococci			
All species	50 (43)	34 (45)	NS
Other than *Staphylococcus epidermidis* or *Staphylococcus haemolyticus*	0	8 (11)	0.001
Enterococcus faecalis	8 (7.0)	1 (1.3)	NS
Viridans streptococci	1 (0.9)	1 (1.3)	NS
Streptococcus agalactiae	5 (4.3)	0 (0)	
Streptococcus pneumoniae	2 (1.7)	3 (4.0)	NS
Subtotal	76 (66)	49 (65)	NS
Gram-negative organisms			
Enterobacteriaceae	13 (11)	10 (13)	NS
Pseudonymous aeruginosa	6 (5.2)	7 (9.3)	NS
Acinetobacter baumannii	10 (8.7)	10 (13)	0.05
Stenotrophomonas maltophilia, Flavobacterium meningosepticum, or *Arcanobacterium haemolyticum*	3 (2.6)	0 (0)	NS
Subtotal	29 (25)	26 (35)	0.05
Fungi			
Overall	10 (8.7)	2 (2.7)	NS
Candida albicans	7 (6.1)	2 (2.7)	NS
Aureobasidium mansoni, Clavispora lusitaniae, or *Rhodotorula rubra*	3 (2.6)	0 (0)	NS

TABLE 2. Risk Factors Associated With Nosocomial Meningitis During the 2 Study Periods

Risk factor	No. (%) of patients, by period		
	1993-1998 (n = 101)	1999-2005 (n = 57)	P[a]
Age of <1 month (neonates)	39 (39)	12 (21)	.04
Cerebral abscess	3 (3.0)	7 (12)	.05
Neoplasia	15 (14.9)	10 (18)	NS
Perinatal pathology or CNS abnormality	18 (18)	3 (5.2)	.02
Neonate with very low birth weight	26 (26)	3 (5.2)	
Neurosurgery or neurological intervention	101 (100)	57 (100)	NS
VPS or other intracranial device insertion or removal	20 (20)	6 (11)	NS
Brain tumor resection	11 (11)	7 (12)	NS
Ventriculostomy	5 (5.0)	5 (8.8)	NS
Craniocerebral trauma or decompressive craniotomy	7 (6.9)	13 (23)	.01
Blood culture positive for pathogen(s), or sepsis	29 (29)	10 (18)	NS
Central venous catheter placed	96 (95)	57 (100)	NS
Total parenteral nutrition	70 (69)	42 (74)	NS
Artificial ventilation	43 (43)	29 (51)	NS
Very low birth weight (<200 g)	33 (33)	29 (51)	.01
More than 1 organism isolated	14 (14)	9 (16)	NS
Prior therapy with broad-spectrum antibiotic	65 (64)	42 (74)	NS
Outcome (prognosis)			
Died	15 (15)	9 (16)	NS
Survived	86 (85)	47 (82)	NS
Without sequelae or relapse	68 (67)	15 (26)	.02
With sequelae or relapse	18 (18)	1 (1.8)	.02
Hydrocephalus with neurosurgery	43 (43)	15 (26)	.05
Inappropriate therapy	6 (5.9)	4 (7.0)	NS
Venous malformation	4 (4.0)	1 (1.8)	NS
Congenital malformations	2 (2.0)	3 (5.3)	NS
Hemorrhage or puncture of hematoma	6 (5.9)	12 (21)	.05
Extirpation of cyst	3 (3.0)	3 (5.3)	NS
Otitis and/or sinusitis	0	4 (7.0)	NS
CSF cultures (>2) positive for pathogen(s)	2 (2.0)	9 (16)	.04
Polymicrobial etiology	18 (18)	20 (35)	NS
No. of cases per 100 neurosurgeries	3.2	2.9	NS[b]
No. of cases / total no. of patient-days	1/2,855	1/2,492	NS[b]

NOTE. CSF, cerebrospinal fluid; CNS, central nervous system; VPS, ventriculoperitoneal shunt.

[a] By χ^2 test (for incidence), except as noted.

[b] By Student t test.

sis–ventriculoperitoneal shunt materials) between the 2 study periods were reported by neurosurgeons.

A comparison of the etiology of meningitis for the 2 study periods revealed that gram-negative bacteria were isolated more commonly during the second study period (26 [35%] of 75 isolates vs 29 [25%] of 115 isolates; $P < .05$) (Table 1). In contrast, fungi were more commonly isolated during the first period (10 isolates [8.7%] vs. 2 isolates [3.0%]). In both periods, the majority of isolates were CoNS (50 isolates [43%] during 1993-1998 vs 34 isolates [44%] during 1999-2004). There was also significant difference among gram-positive pathogens. Eight cases of meningitis (11%) during the second study period were caused by non–*Staphylococcus epidermidis* CoNS (such as *Staphylococcus warneri, Staphylococcus hominis, Staphylococcus cohni,* and *Staphylococcus haemolyticus*), whereas no cases of meningitis were caused by these pathogens during the first study period ($P < .01$). All 10 non–*S. epidermis* CoNS strains were resistant to methicillin (minimum inhibitory concentration, >8 μg/mL), and 6 were also resistant to teicoplanin (minimum inhibitory concentration, >16 μg/mL); 20 cases of meningitis (35%) in the second study period had a polymicrobial etiology (CoNS and *P. aeruginosa* or CoNS and *A. baumannii*)

The following gram-negative bacteria were isolated more frequently during the second study period: *A. baumannii* (10 isolates [13%] vs 10 isolates [8.7%]) and *P. aeruginosa* (7 isolates [9.3%] vs 6 isolates [5.2%]). Three of 10 Enterobacteriaceae organisms were resistant to cefepime, and 2 of 7 *P.*

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aeruginosa isolates were resistant to meropenem (Table 2). DNA fingerprinting was not performed, but clusters of resistance patterns were not detected in resistance phenotypes.

There was no significant difference in mortality between the 2 study periods. However, there was a significant decrease in the frequency of neurologic complications (eg, hydrocephalus, palsy, and epilepsy) during 1999–2004, compared with 1999-2004 (1.8% vs 18%; $P < .01$). In contrast, cerebral abscess was a complication of meningitis more frequently during 1999-2004 (7 cases [12%] vs 3 cases [3%]; $P < .05$). The following risk factors were more common during the second study period: sinusitis-otitis (4 [7.0%] vs 0; $P < .05$) and craniocerebral trauma (13 [23%] vs 7 [6.9%]; $P < .01$). Perinatal pathologic conditions and abnormalities of the central nervous system (18 cases [18%] vs 3 cases [5%]; $P < .02$) and very low birth weight (26 [26%] vs 3 [5%]; $P < .002$) were more common during the first study period. The incidence of meningitis per 100 neurosurgeries and the incidence per 1,000 patient-days were not significantly different between the study periods (Table 2).

There were no major changes in the etiology of nosocomial meningitis between 1993-1998 and 1999-2004. Although the incidence of cases due to *P. aeruginosa* and *A. baumannii* increased, the increase for gram-negative bacteria overall was not significant (35.5% vs 25.3%). During the second study period, one-third of all Enterobacteriaceae isolates were resistant to fourth-generation cephalosporins, and 28% of *P. aeruginosa* isolates were resistant to meropenem. The prevalence of teicoplanin resistance among coagulase-negative staphylococci (more than 10%) was alarming: resistance to this drug was detected in 12 strains of *S. epidermidis, S. haemolyticus, S. warneri,* and other CoNS.

Although the mortality rate remained relatively unchanged (16% in 1999-2005 vs 15% in 1993-1998), the percentage of patients with neurologic sequelae decreased during the second study period ($P < .02$), probably because the percentage of inappropriately treated patients decreased from 20% (20 of 101) to 10% (6 of 57).

Increases in the incidence of sinusitis-otitis (among patients who underwent ear-nose-throat surgery) and craniocerebral trauma (as an underlying disease) were observed during the second study period. This suggests that inadequate antibiotic therapy administered to patients with craniocerebral trauma and to those who underwent ear-nose-throat surgery might have caused meningitis or brain abscess. In contrast, the incidence of meningitis dramatically decreased after 1998 among neonates with a very low birth weight (from 25.6% during 1993-1998 to 5% during 1999-2004), probably because the combination therapy (ampicillin plus gentamicin) used before 2000 was replaced by more-appropriate antibiotic therapy (a third-generation cephalosporin plus ampicillin).[1-2]

Death remains a complication of nosocomial meningitis in children who have undergone neurosurgery (mortality rate, 10%-15%). Because the susceptibilities of *P. aeruginosa, A. baumannii,* and CoNS are unpredictable, in vitro susceptibility testing seems to be mandatory to ensure that appropriate treatment is administered: in our study, susceptibility testing was associated with favorable outcome, decreased mortality, and fewer neurologic sequelae. Because of increases in the prevalence of antibiotic resistance and in the infection-associated mortality due to the inappropriate use of empirically administered antibiotics, adherence to recommended infection control and prevention practices (including proper disinfection and sterilization techniques and appropriate use of antimicrobial perioperative prophylaxis) and skillful performance of surgery are mandatory.

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